~~Nov~~ DEC 2, 1998

Ltr 12/8/98

Quarterly Progress to:	National Institutes of Health
Contract Monitor:	William Heetderks, Ph.D.
Research Contract:	"Surface Modification for Biocompatibility"
Contract No.:	NS 5-2322
Principal Investigators:	David C. Martin and K. Sue O'Shea
Date:	October 31, 1998

Overview

This report is a summary of our activities in the third quarter of the year-long no-cost extension of our contract, corresponding to the third quarter of 1998. In this fifteenth period of our activities, we have continued to investigate variations in polymer processing and characterization, as well as to model the mechanical behavior of neural prosthetic probes implanted into soft tissue. This report provides an overview of the major results to date and discusses our plans for the future.

Polymer Processing and Characterization

In this past quarter we have been extending our ability to construct filamentous microstructures of polymers using electric-field mediated deposition techniques (electrospinning). We have been developing schemes to control the out-of-plane density gradients by spinning from solutions using AC potentials, and by spinning directly onto the surface of a coagulating bath. These techniques have been used on the genetically engineered bioactive proteins, as well as on aliphatic and aromatic synthetic polyamides.

The proven feasibility for spinning fibers directly onto a water bath has important implications for the surface modification of probes with living cells. This suggests that a means for trapping candidate cells onto the surface of a device will be to coat the probe with the cell media and then spin fiber down as a mesh-like net which will hold them in place on the substrate. For this process to be successful, it will likely be necessary to have a larger distance of separation between the syringe and the substrate to insure volatilization (greater than 2 cms).

The ability to introduce oscillating voltages provides for additional control over the fibrous polymer morphology. Fig 1. shows a mat of electrospun aliphatic polyamide filaments with a uniform diameter, using 8 kV DC potential and a 2 cm separation distance. Figure 2 shows a film created under conditions where there are now droplets on the strings, provided by an 8 kV DC field with a superposed AC sine wave of 2 kV at a frequency of 100 Hz and a separation of 3 cm. Figure 3 shows a more well developed droplet texture, now created with similar conditions as in Figure 2 but with a frequency of 1000 Hz It is reasonable to presume that these variations in structure will lead to differences in mechanical properties of the filamentous mats.

Figure 4 shows a mat of electrospun polymer filaments on the surface of a silicon substrate. The mat is over 20 microns thick, and the outermost regions are of very low density, with individual filaments seen extended above the solid surface. The mat increases in density near to the silicon substrate. This morphology is consistent with the expected need to accommodate mechanical properties variations from the solid, stiff device to the softer living tissue.

Plans:

Michael Johnson is working to complete his dissertation within the next year. A new student, Xianyan Cui, from the Macromolecular Science and Engineering center, currently supported by a TA from the Chemistry department, has started to work with Prof. Martin and is also interacting with Prof. O'Shea and Prof. Eric Shelden. Prof. Shelden is examining the interaction of fibroblasts with woven mats of various polymer materials prepared in our laboratory.

Bioactivity of Protein Polymer Films *in vivo*

An addiitional series of probes were coated with SLPL, SLPF, and SELP, and were implanted into Guinea Pig CNS, in collaboration with Richard Altschuler, Jim Wiler, and Peter Finger of the Kresge Hearing Research Institute. Quantitative histological studies will be performed after 3 weeks of implantation and compared with our previous results.

Finite Element Modeling of the Mechanical Behavior of Probes in Tissue

Finite Element models have been constructed using IDEAS v3.0 and analyzed using ABAQUS v5.5 in order to evaluate the implications of probe geometry and the efficacy of coatings for influencing the deformation behavior of the stiff probes in soft tissue. The models were constructed by estimating the geometry of the probe, the CNS, and providing estimates of the mechanical properties as available from measurements in our laboratories and the literature.

Figure 5 shows the geometry of probe used in the simulation. The figure is shaded to reflect the variations in modulus between the different components. The parameters used in the simulations are shown in Figure 6. Two different deformation modes were used: "shear", in which the boundaries around the probe and brain were kept rigid and then translated laterally with respect to one another, and "poking", in which the two sides of the simulation were moved both toward and away from one another.

Figures 7, 8, 9, and 10 show the influence of the modulus of the probe and the influence of adhesion between the probe and the tissue on the expected deformation field. The plots show the displacement of the nodes after the distortion, and the colors correspond to variations in the largest invariant of the stress tensor as a function of position around the probe. For the stiff probe with no adhesion, there is a buckling of the pia, and a delamination of the probe away from the tissue (Figure 7). With improved adhesion, the delamination is reduced, but there is still local buckling of the tissue. When the probe is softened, there is considerably less tissue deformation, regardless of whether the adhesion is strong or weak (Figures 9 and 10). The local strains near the probe tip were found to be most severe during the "poking" mode of deformation, rather than in shear.

Outside Communications and Collaborations

Dr. Allen Mensinger from Washington University has reported that SLPL/NGF coated probes provide improve performance when implanted into toadfish. Histological results show an increased number of neurons regenerated on the coated probes. Furthermore, the coated probes retain their ability to transmit electrical signals.

Daryl Kipke and Andy Schwartz from Arizona State University reported that the wire bundles we coated for them did not produce meaningful results, although this did not appear to be associated with a problem with the coatings.

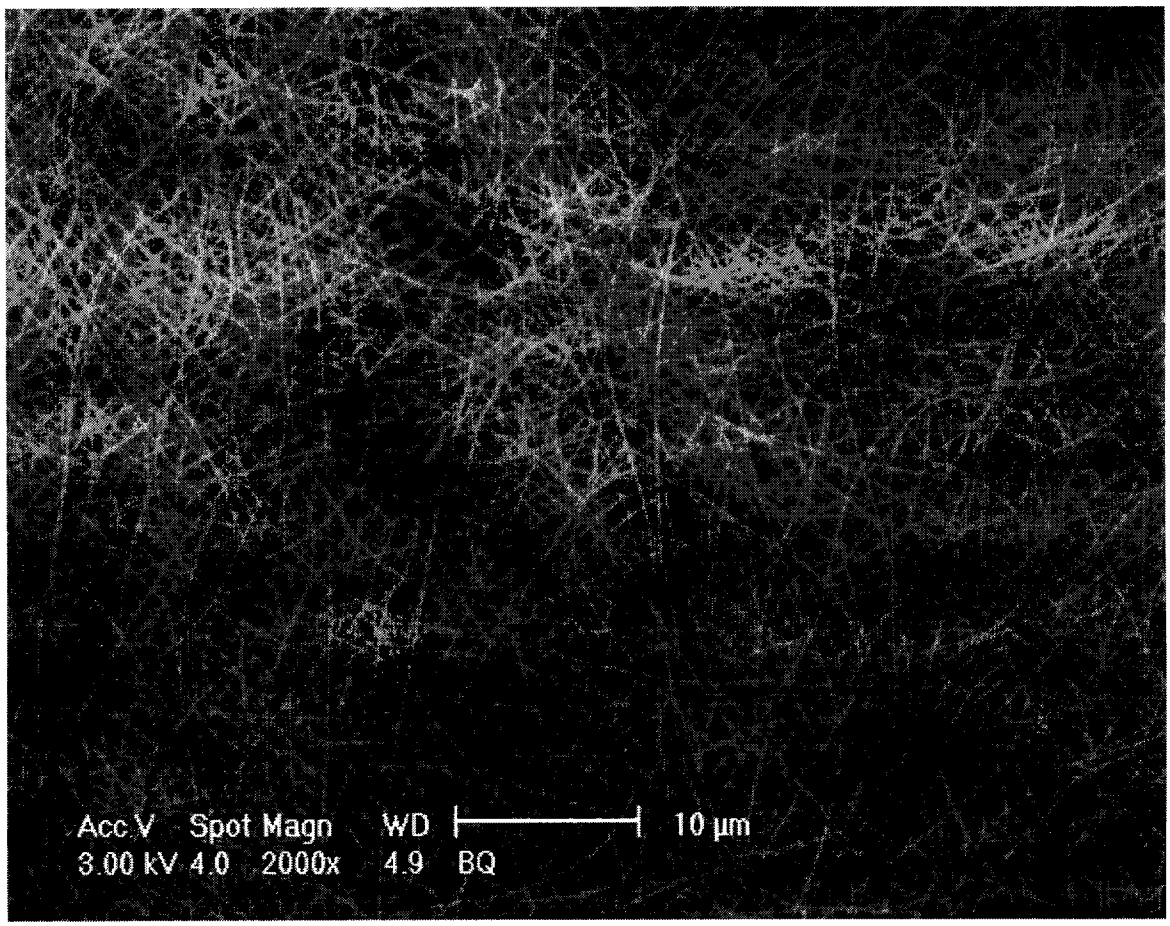

Fig. 1

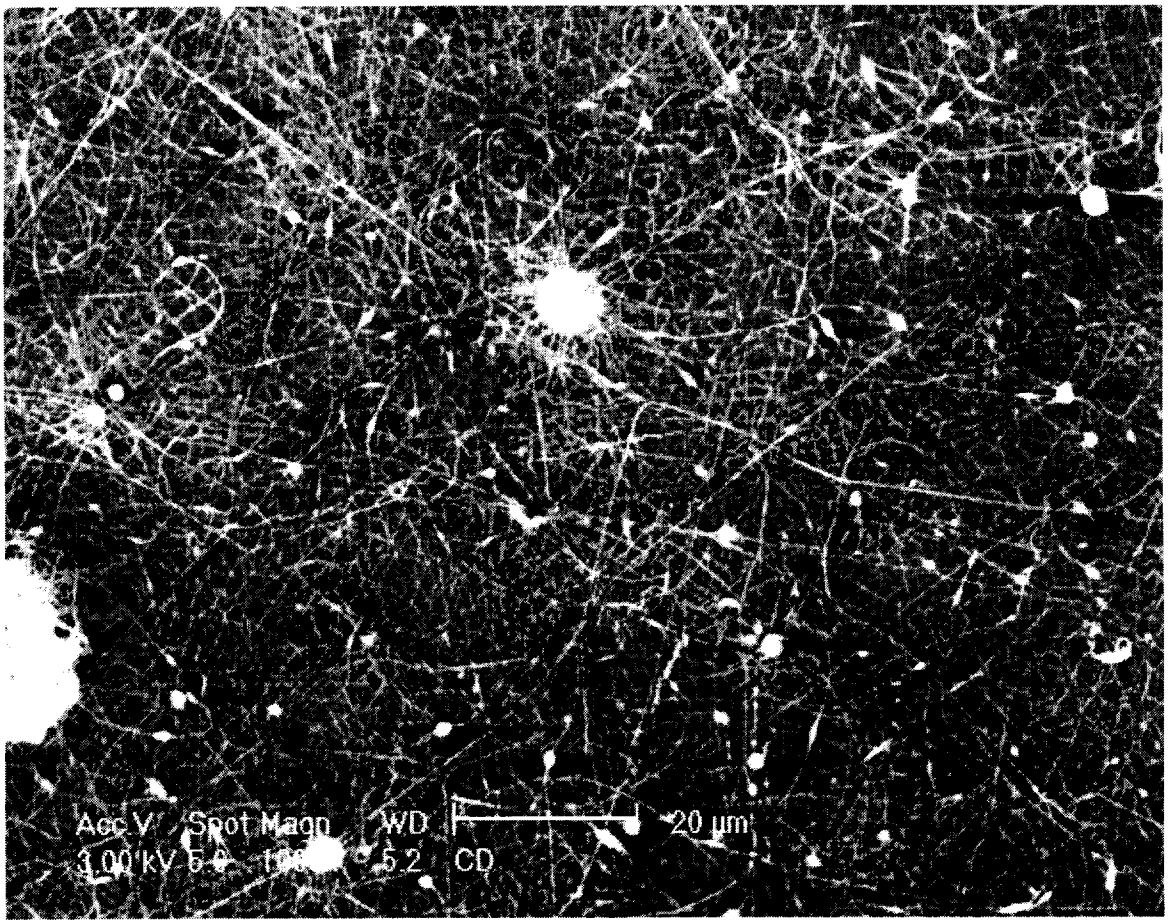

Fig. 2

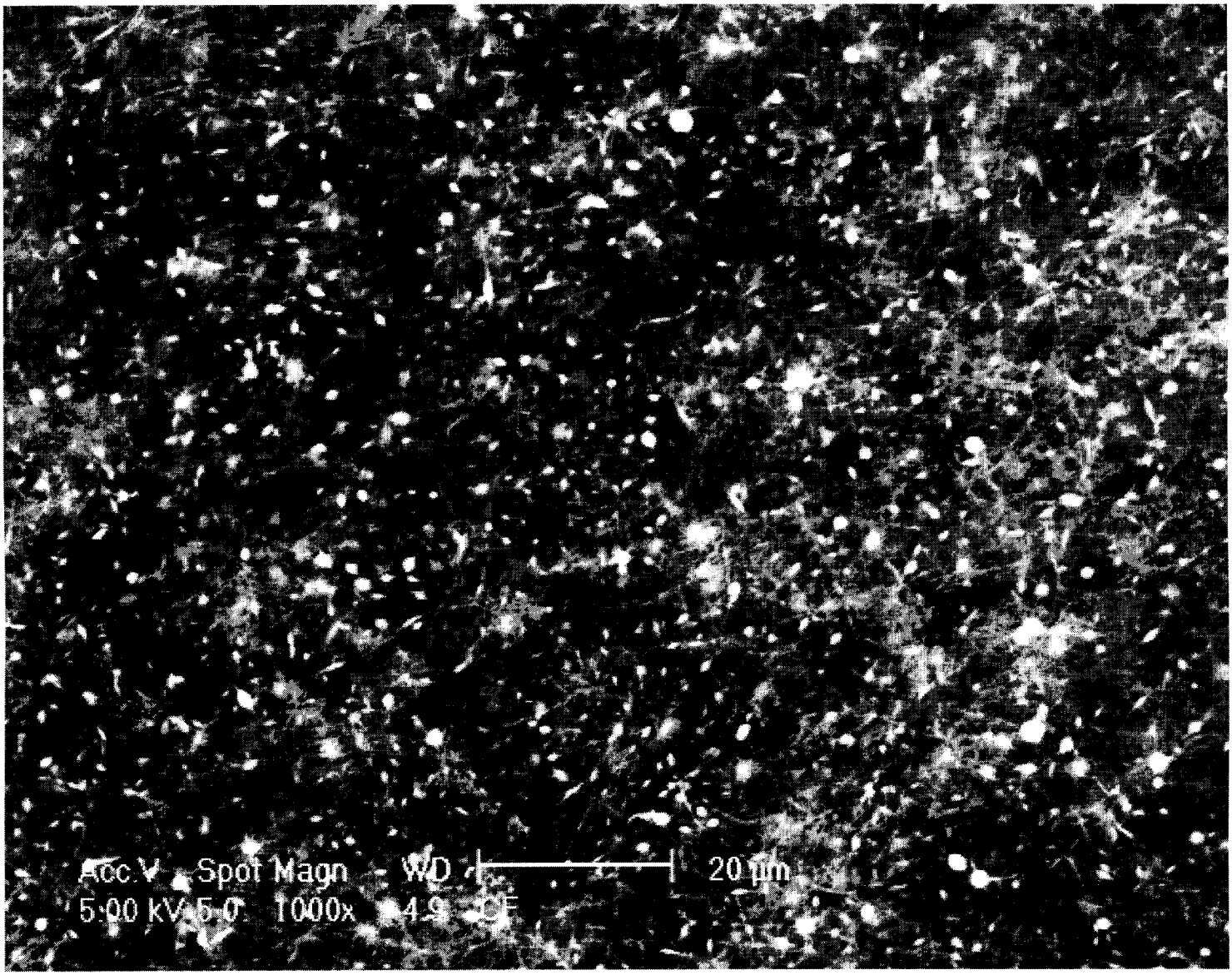

Fig. 3

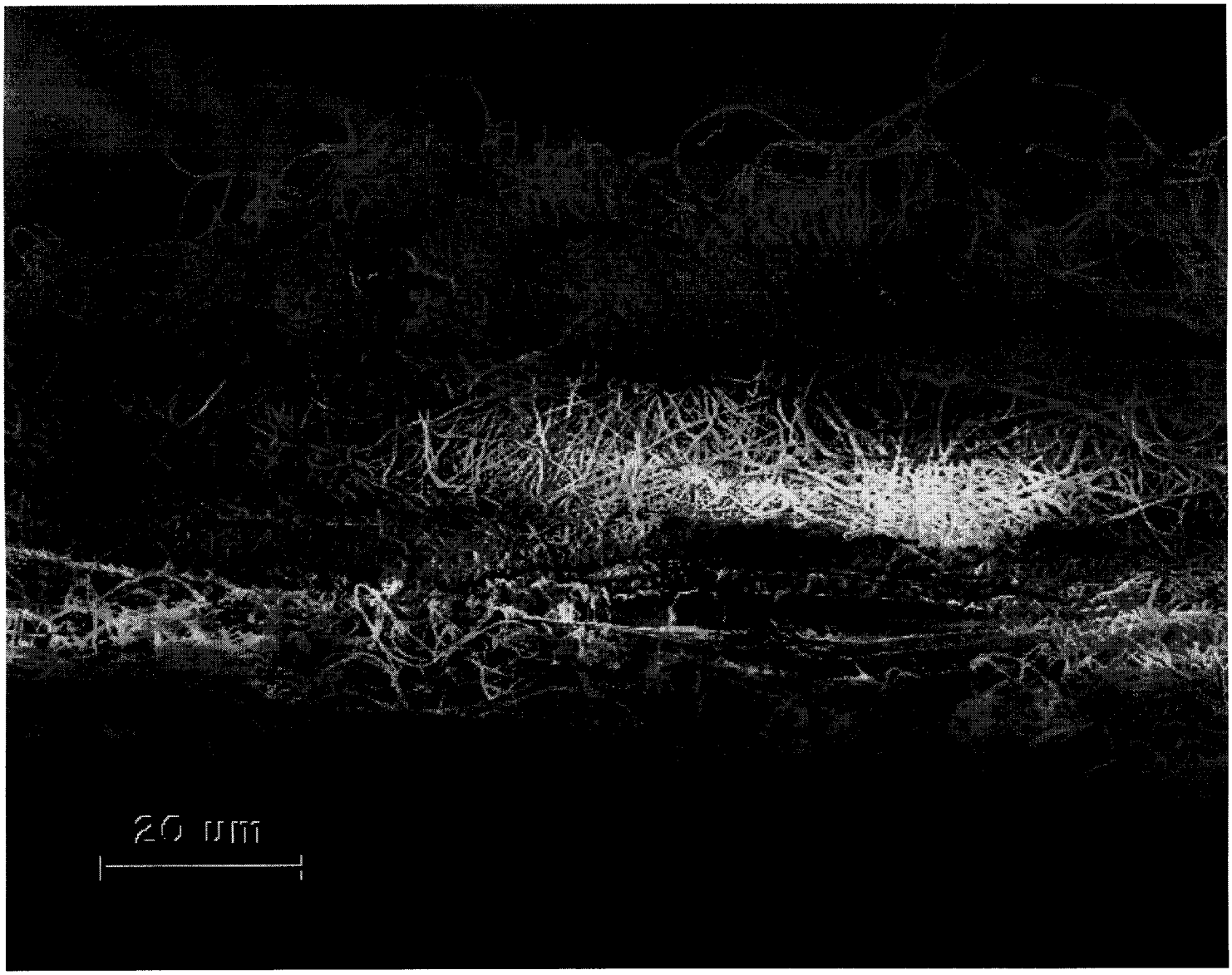

Fig. 4

Finite Element Model of Probe in Brain

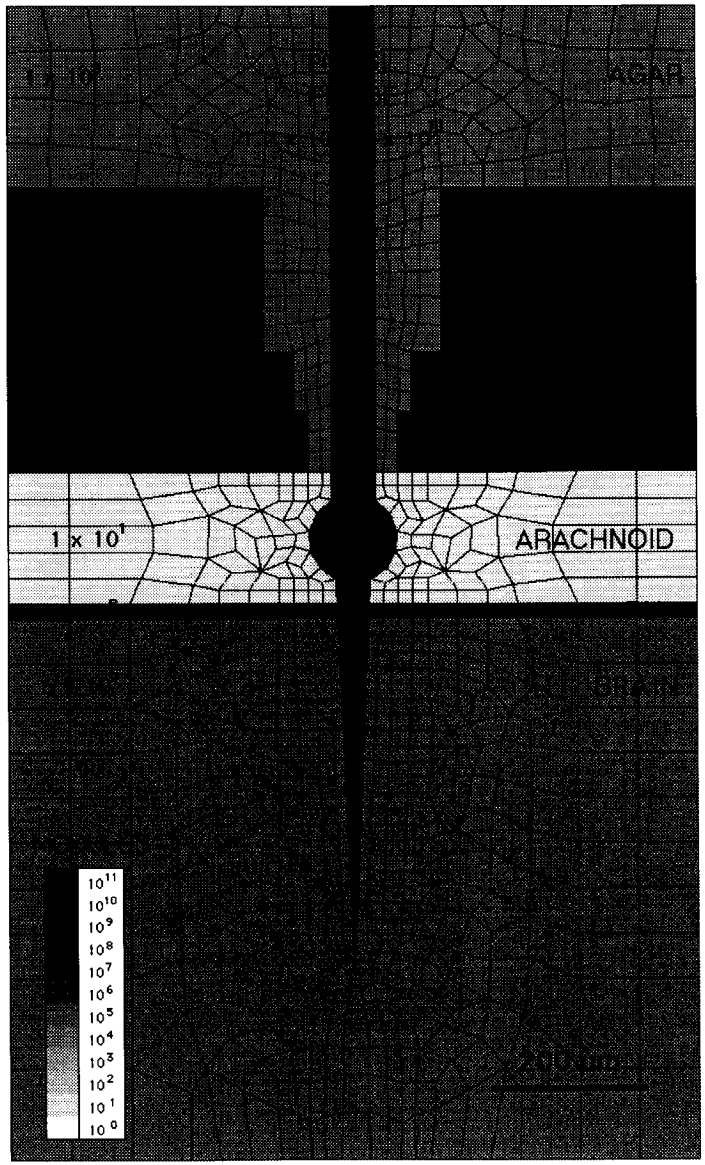

Fig. 5

- Bulk modulus of various tissues and materials in finite element model.
- Deformation simulated by movement of brain and pia against skull tissues and probe.

Finite Element Model of Probe in Brain

- Model Building
  - **IDEAS v.3.0**
- Model Simulation
  - **ABAQUS v. 5.5**
- 1156 nodes, 1074 elements, four-node shell type.
- 2-dimensional model, boundaries have restricted z and torsional movement.
- Model edges fixed into two sets, one set moved relative to the other to simulate brain movement.
- Shear and poking modes of deformation.
- 10 equal increments to final the deformation of 2% model dimension.
- Output elemental stress and strain, plots show strain.

Finite Element Model of Probe in Brain

- Difference in deformation from probe material:
  Silicon, Poor interface

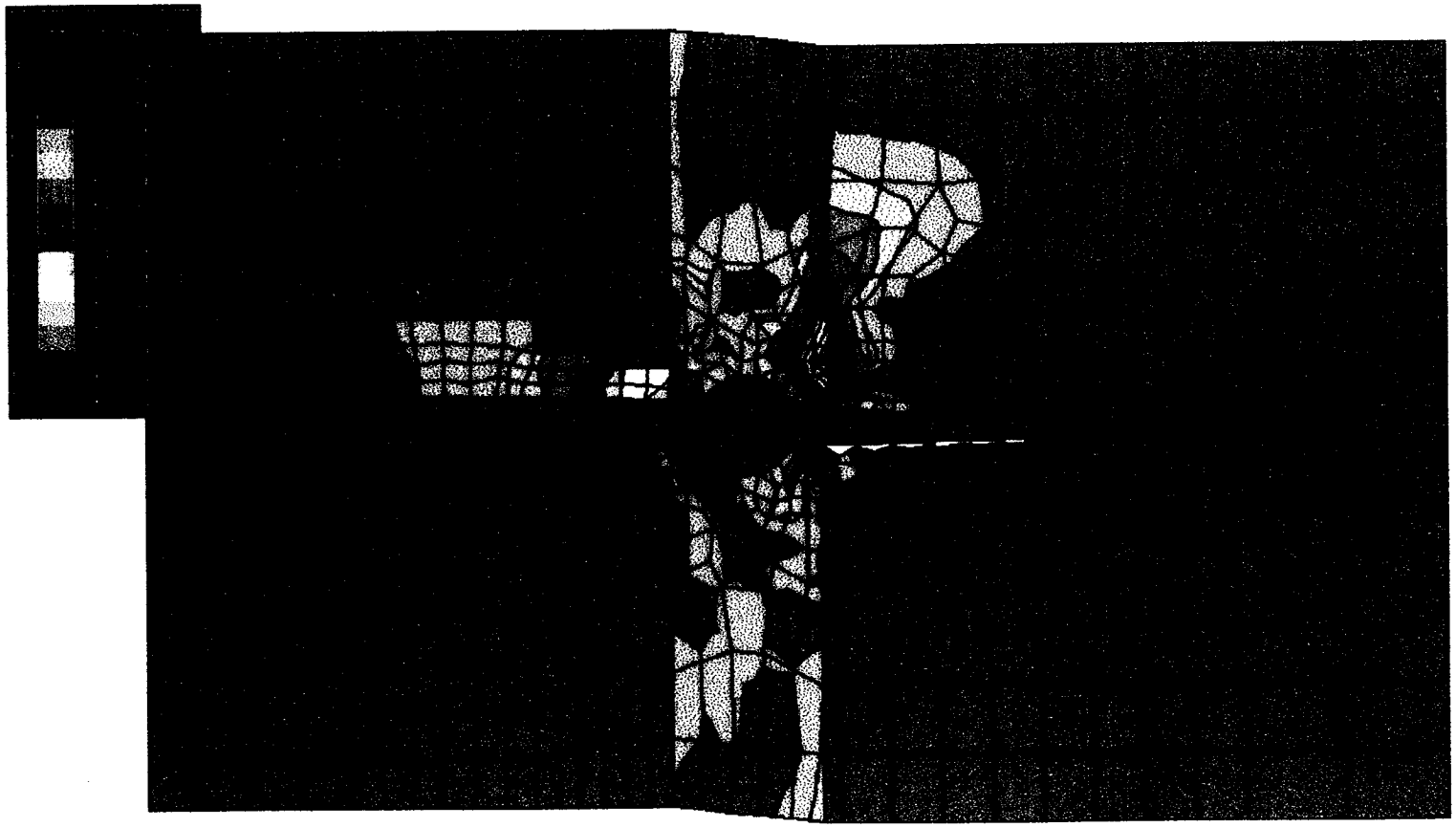

Fig. 7

Finite Element Model of Probe in Brain

- Difference in deformation from probe material:
  Silicon, Strong interface

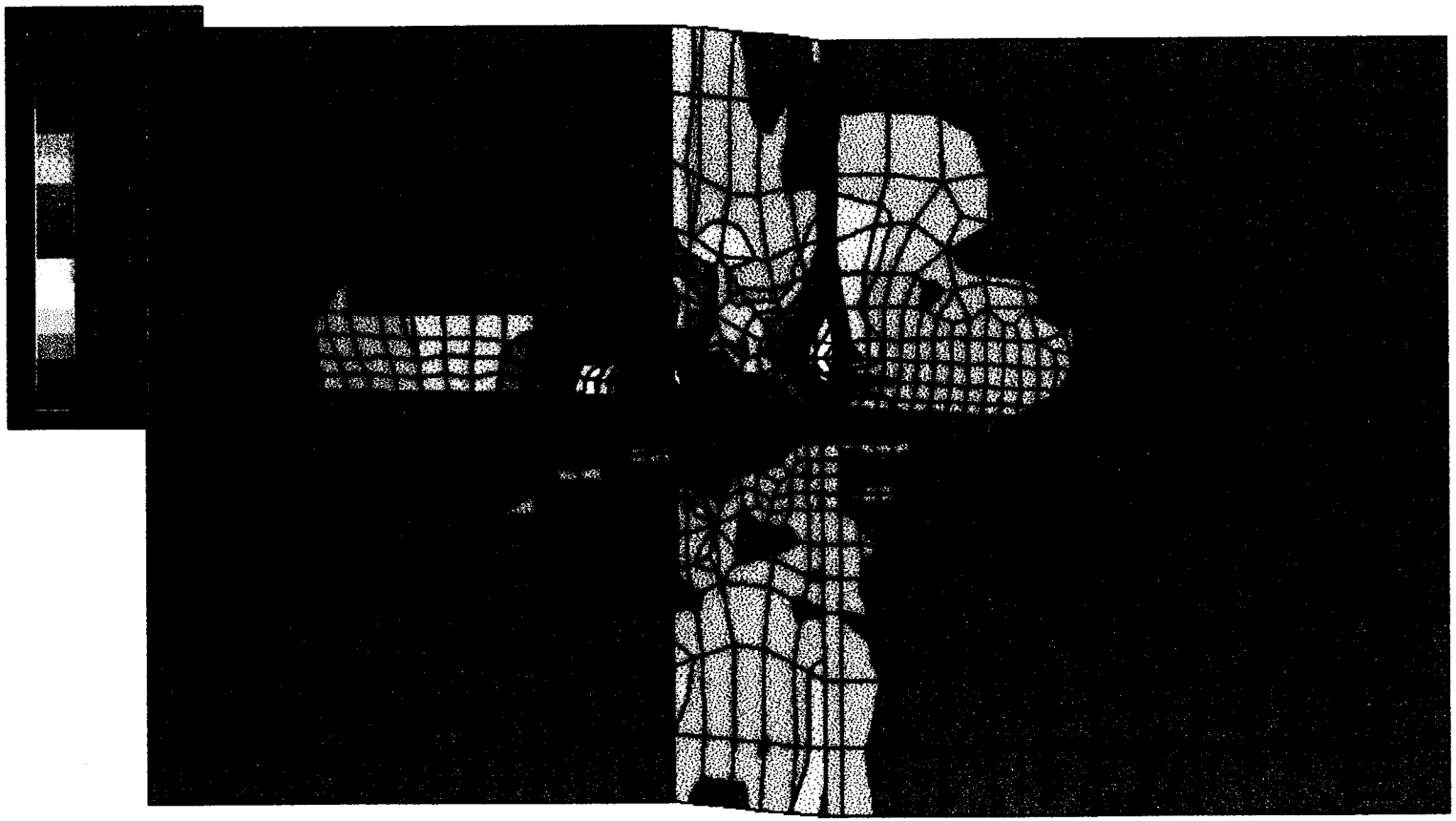

Fig. 8

Finite Element Model of Probe in Brain

- Difference in deformation from probe material:
  Polypropylene, Poor interface

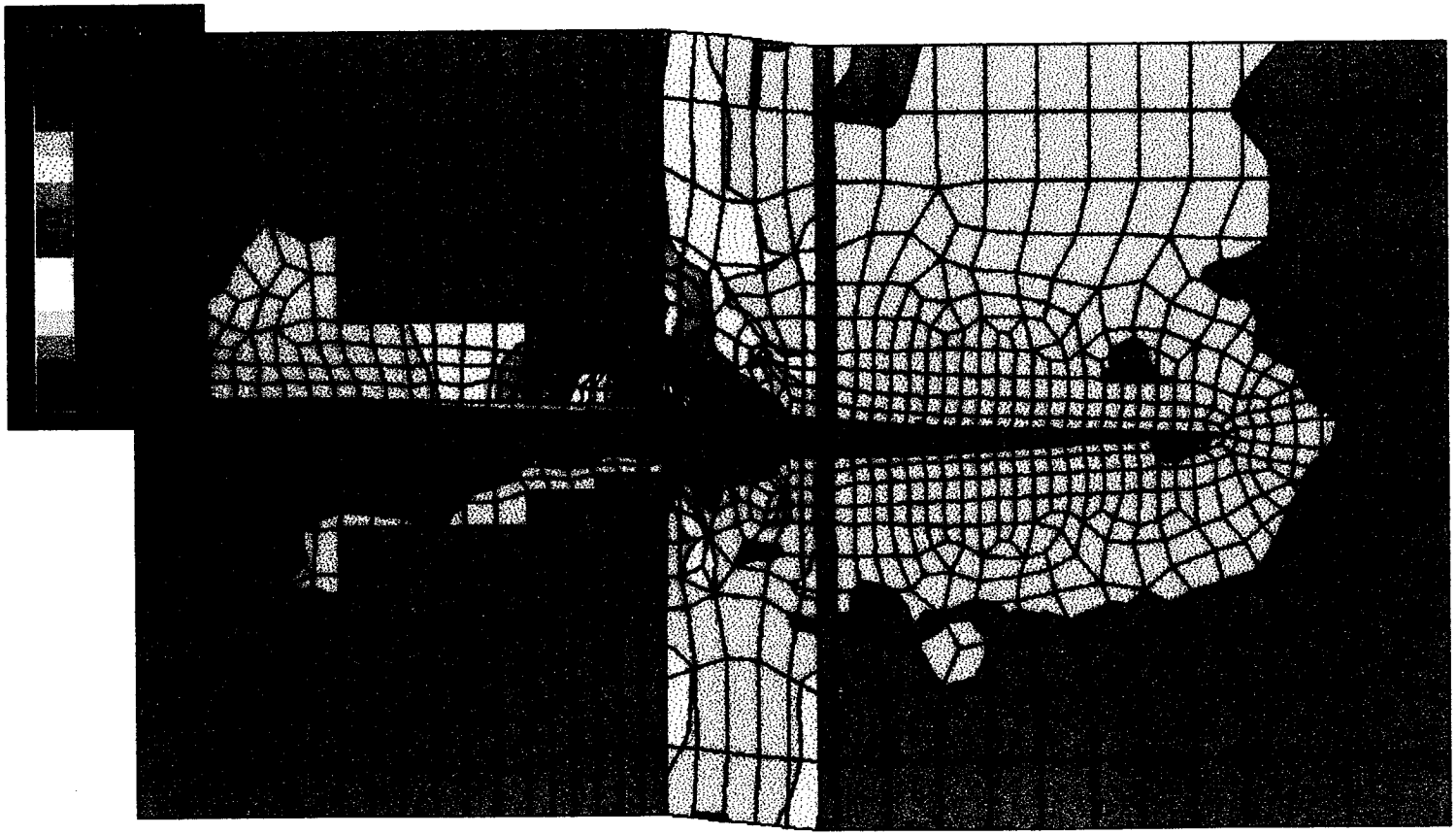

Fig. 9

Finite Element Model of Probe in Brain

- Difference in deformation from probe material:
  Polypropylene, Strong interface

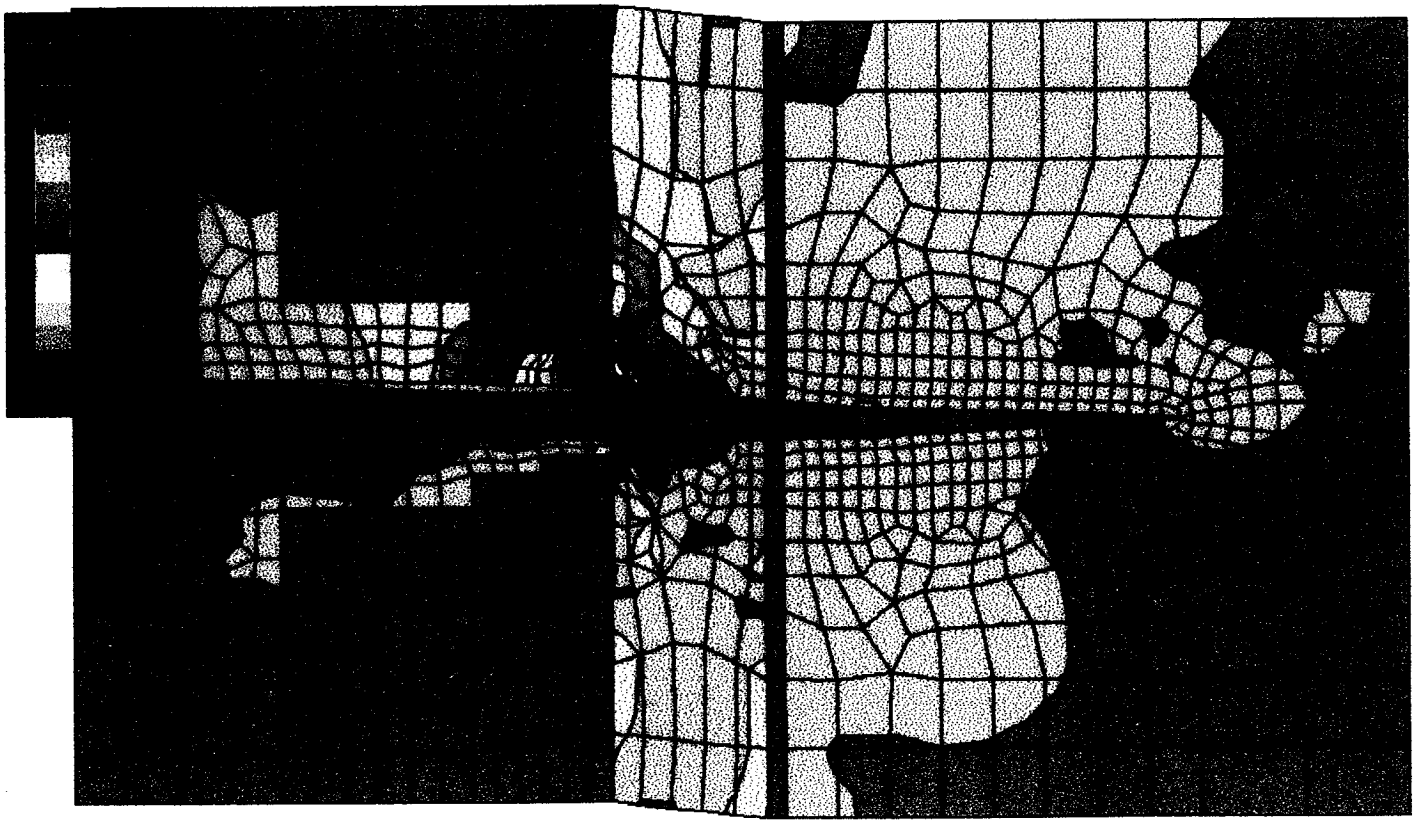

Fig. 10